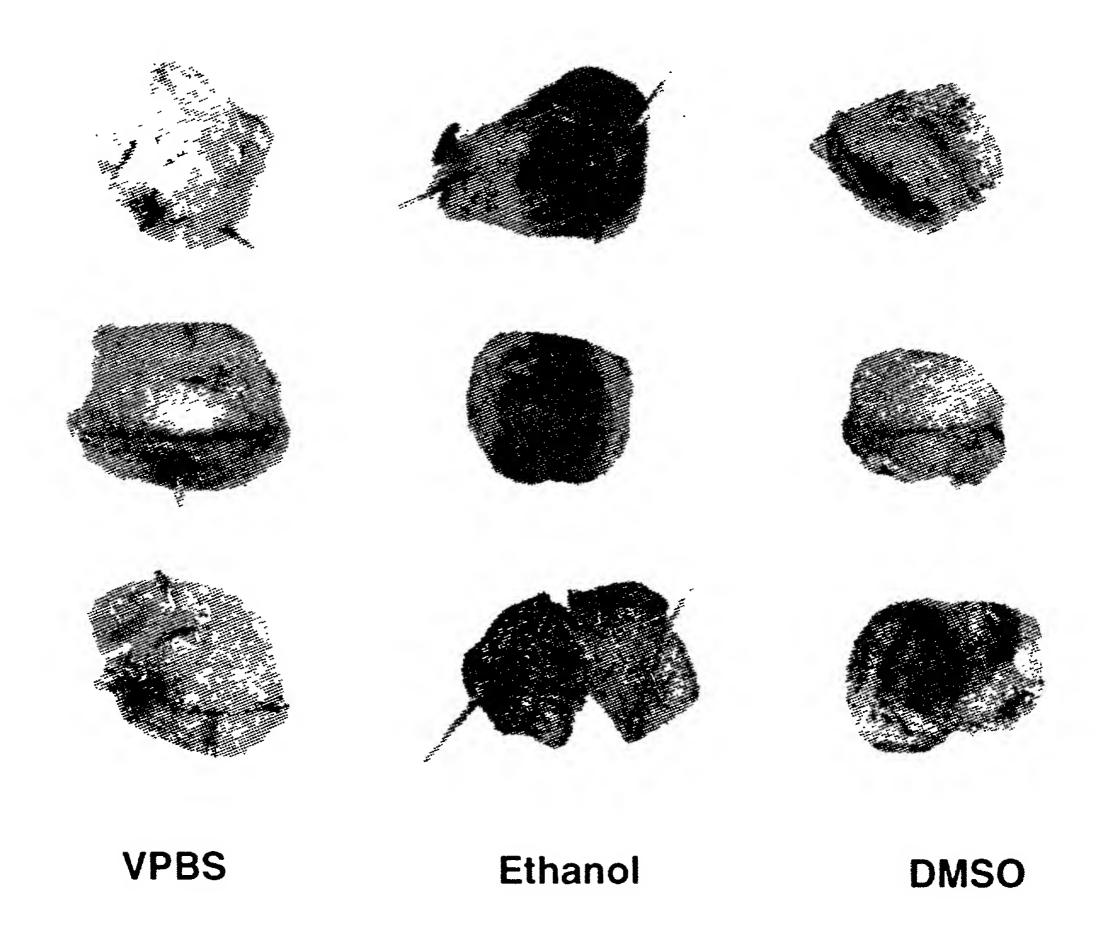
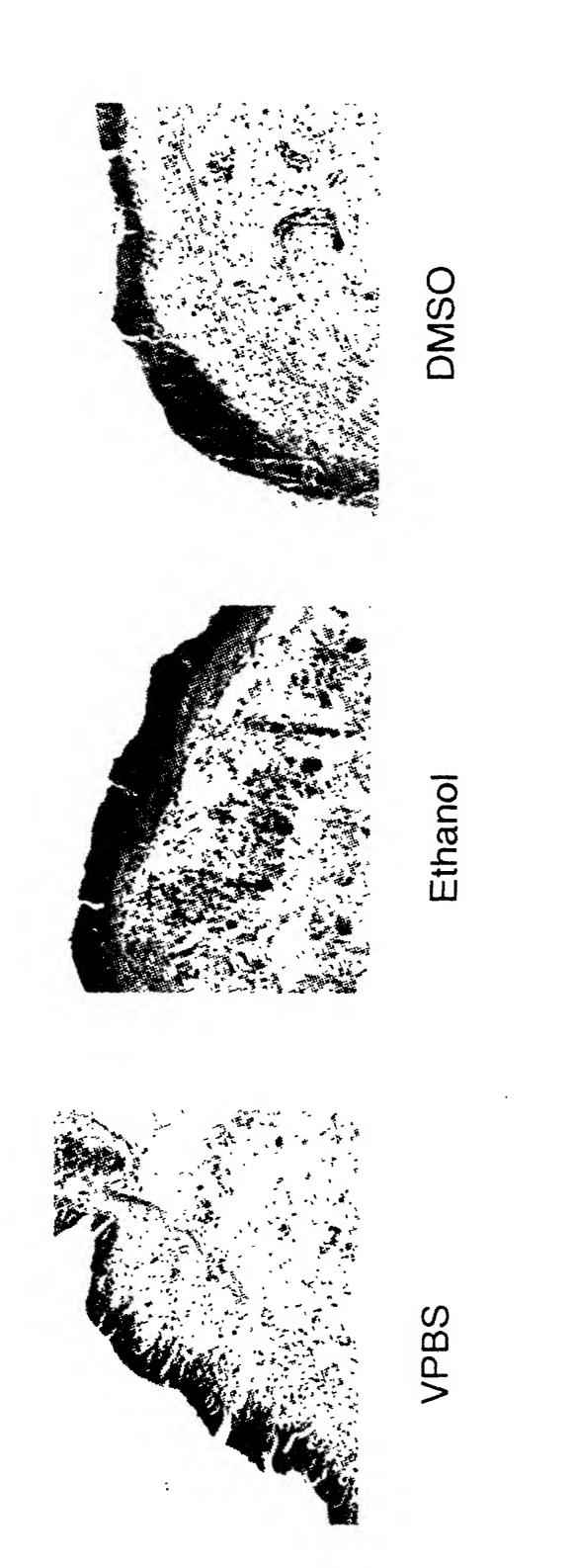
Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 1 of 35



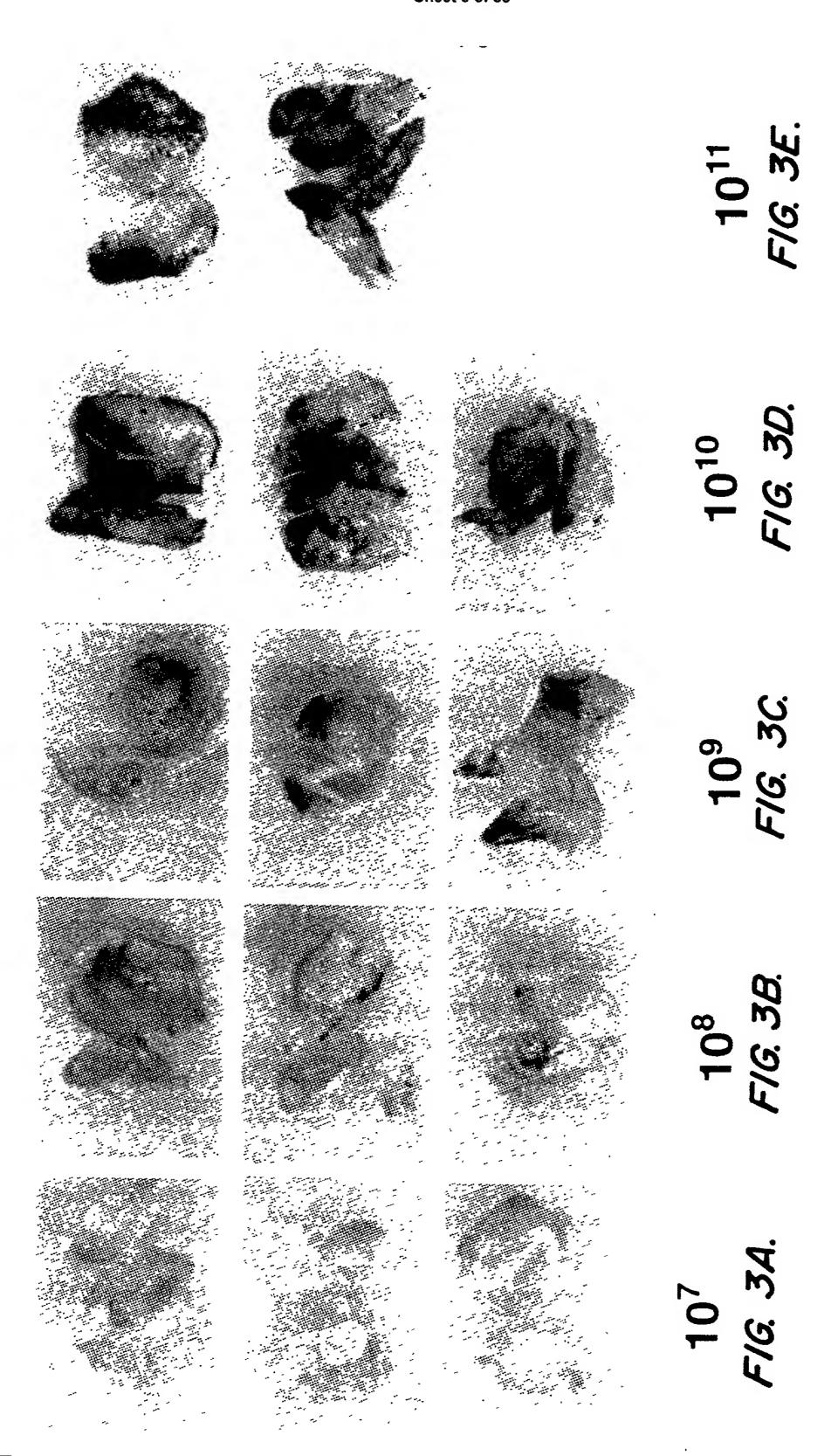
F1G. 1.

Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 2 of 35



76. 2.

Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 3 of 35



Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF

THERAPEUTIC AGENTS TO CELLS
Sheet 4 of 35

CONTROL
CONTROL
CONTROL
CONTROL
ACNRB (VPBS)
ACNRB (ETHANOL)
B-actin (PBS)
B-actin (ETHANOL)



F/G. 4.

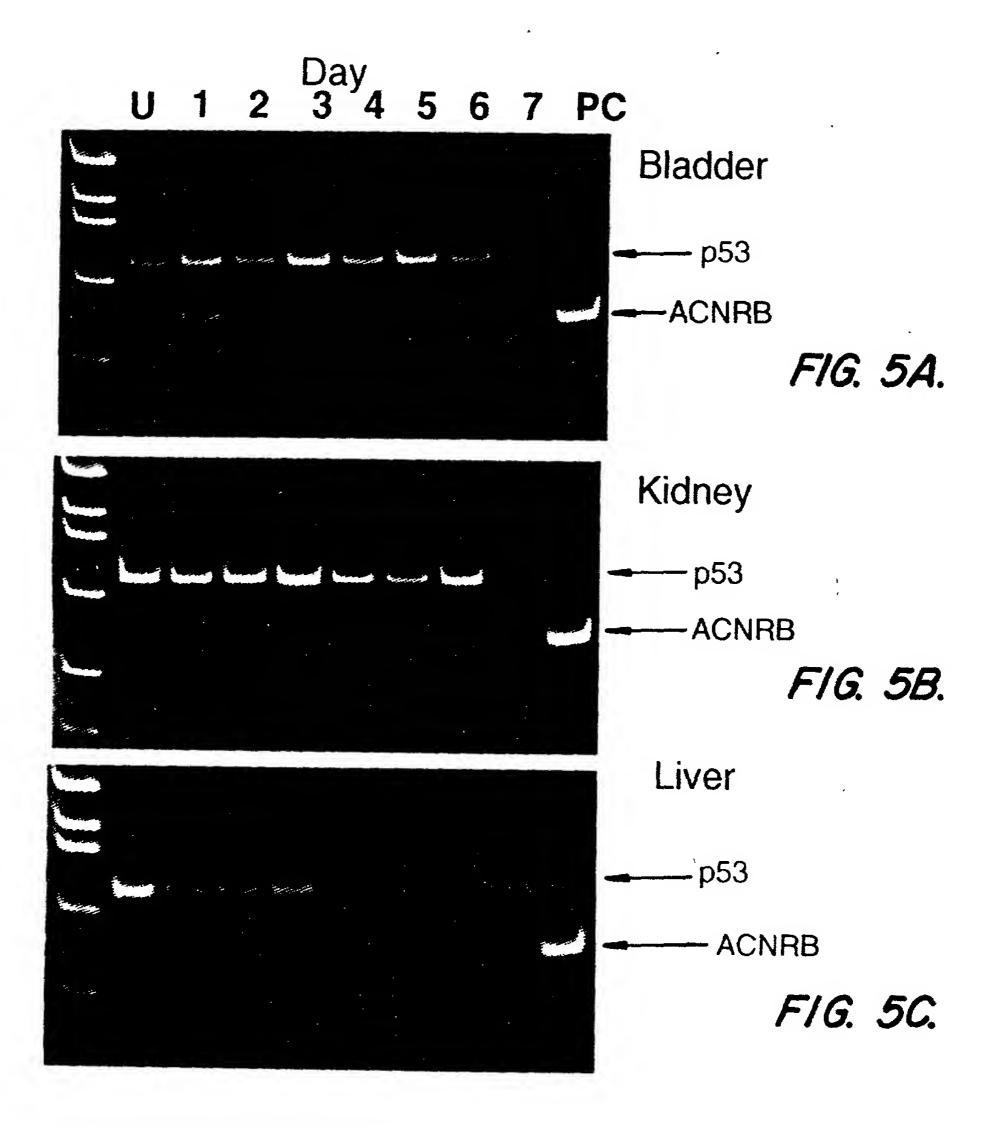
+

Atty. Docket No.: 016930-000816US

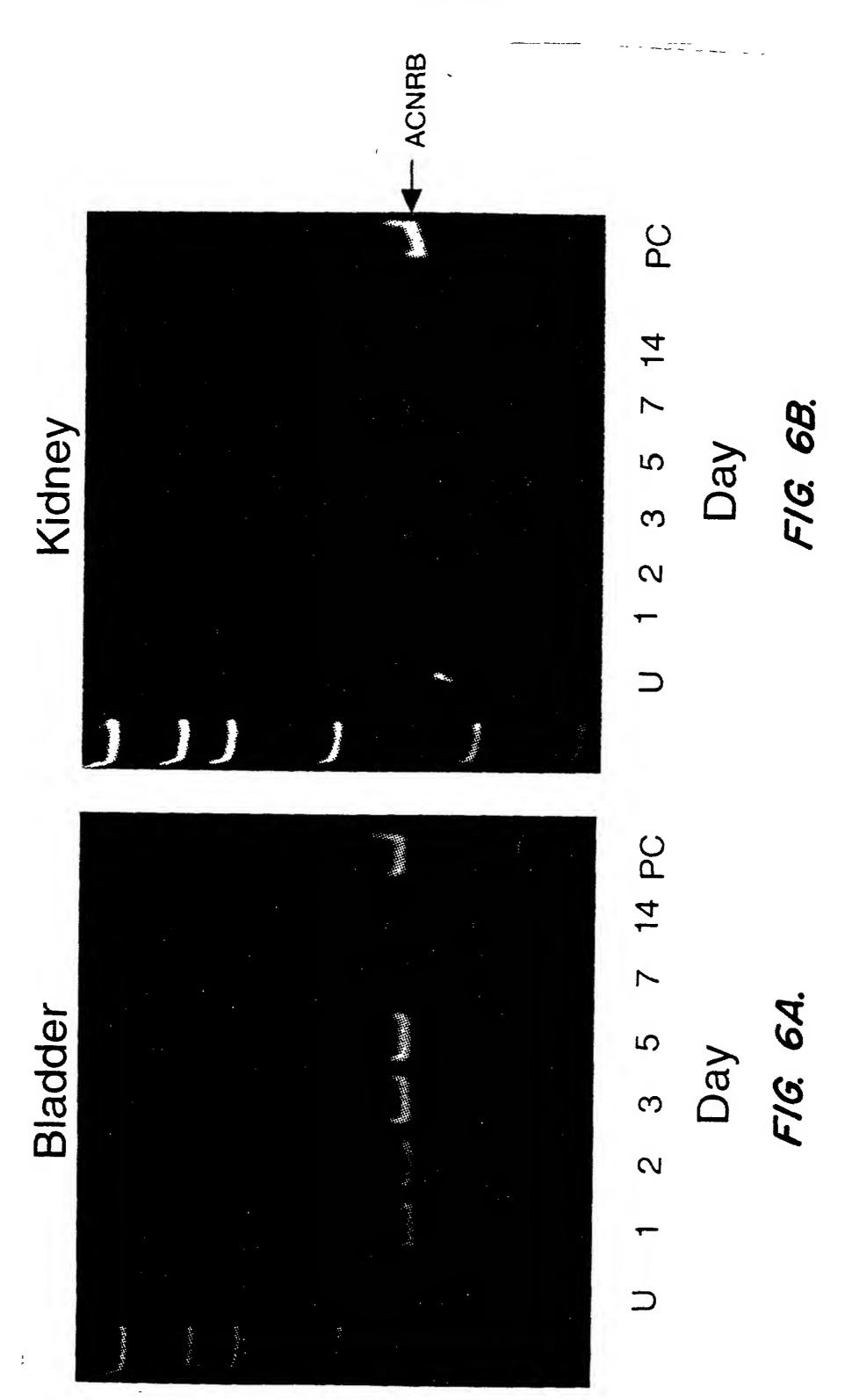
Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 5 of 35



Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 6 of 35



Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 7 of 35

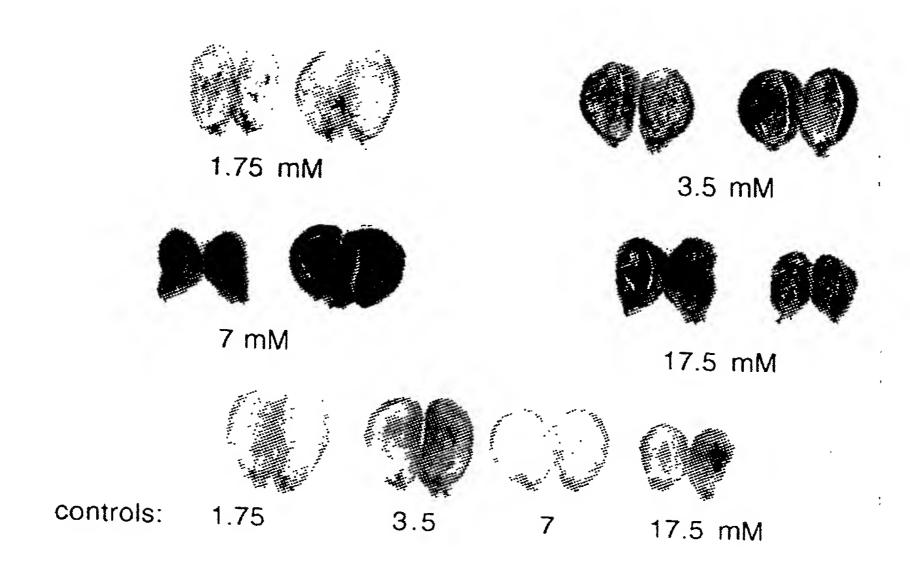
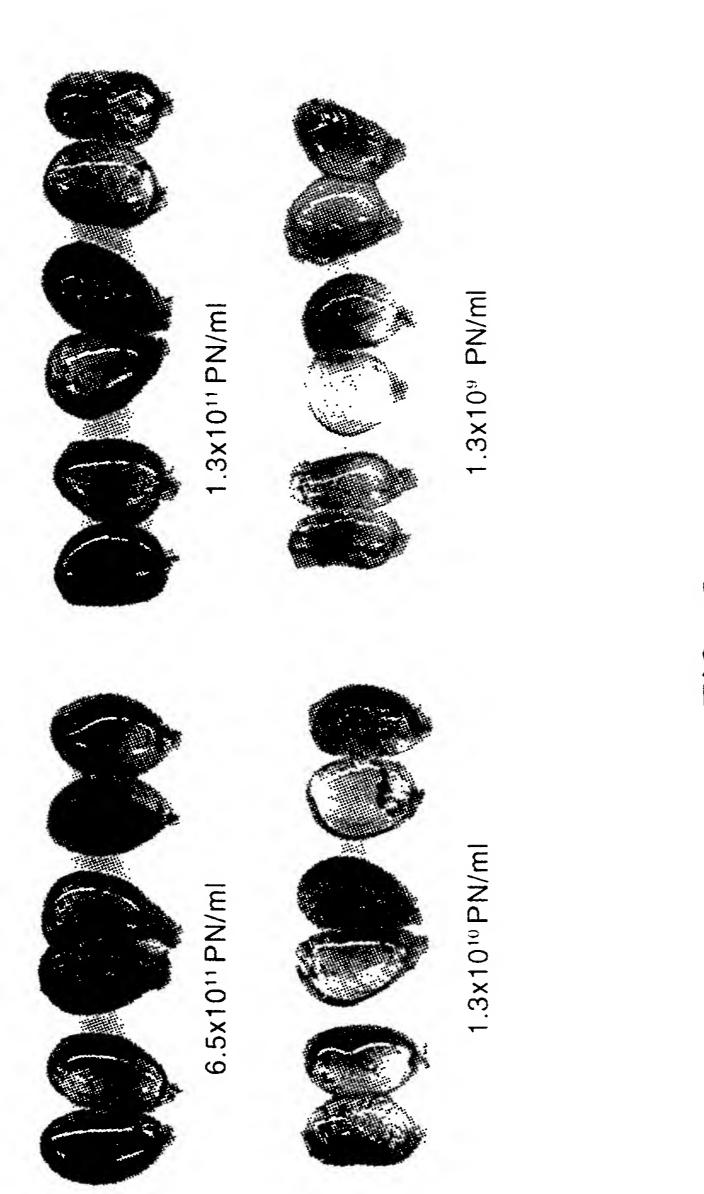


Figure 7

Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF
THERAPEUTIC AGENTS TO CELLS
Sheet 8 of 35

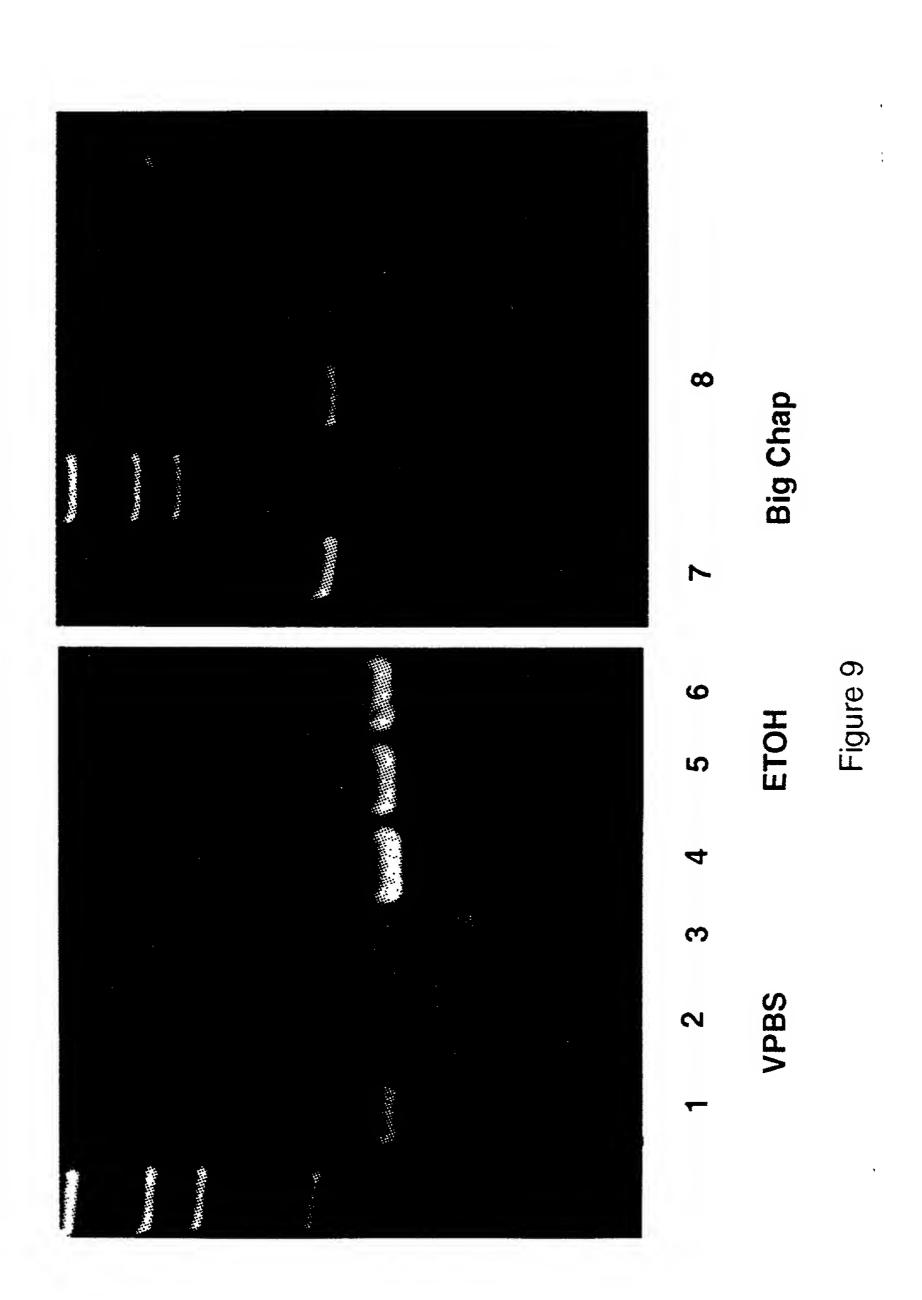


Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 9 of 35



Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

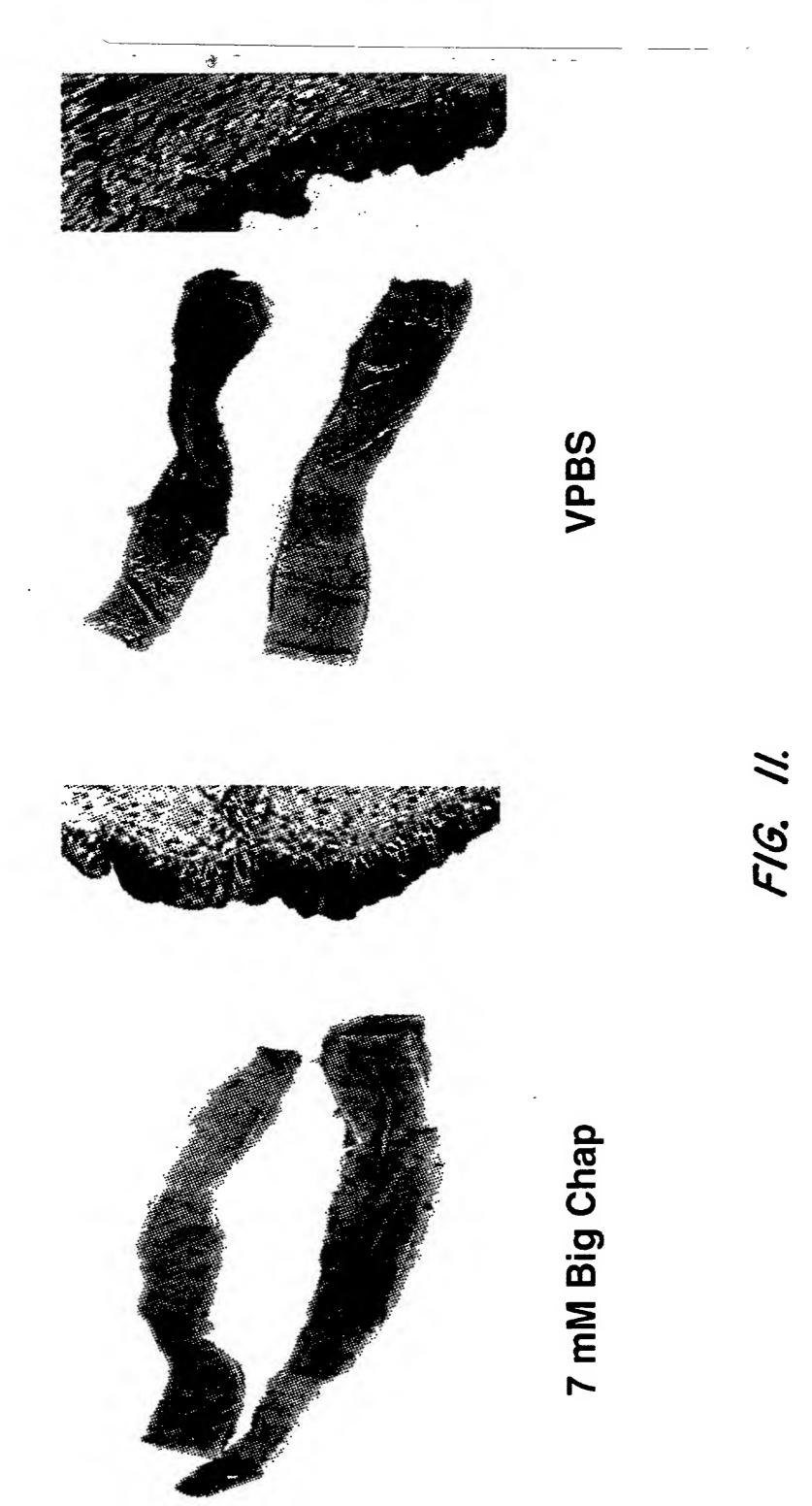
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 10 of 35



Big Chap (4 mM)

Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF
THERAPEUTIC AGENTS TO CELLS
Sheet 11 of 35



Atty. Docket No.: 016930-000816US

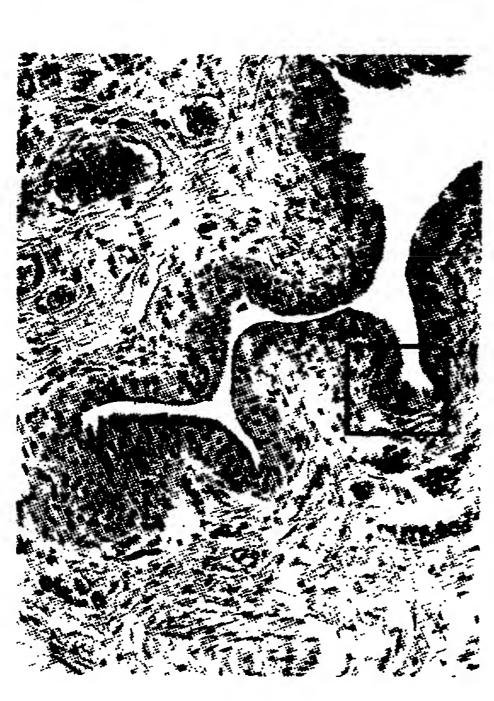
Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 12 of 35

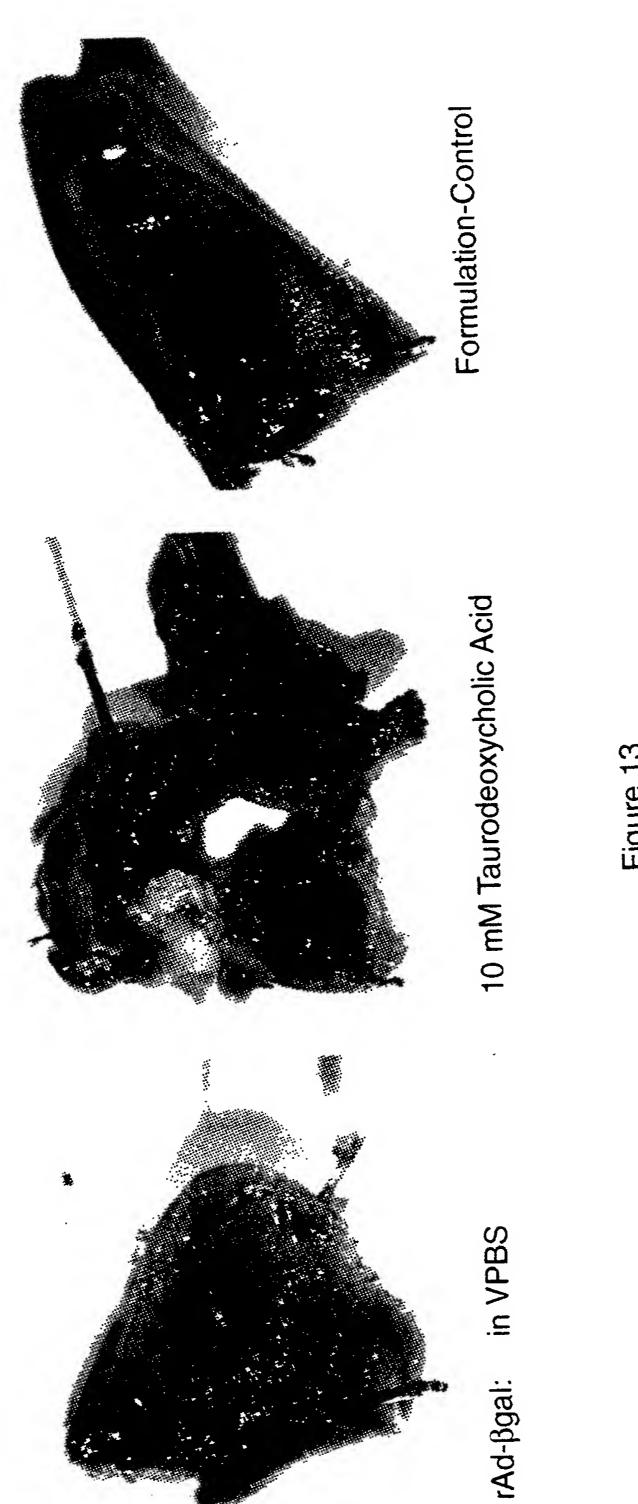


1200 X



F16

Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 13 of 35



Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 14 of 35

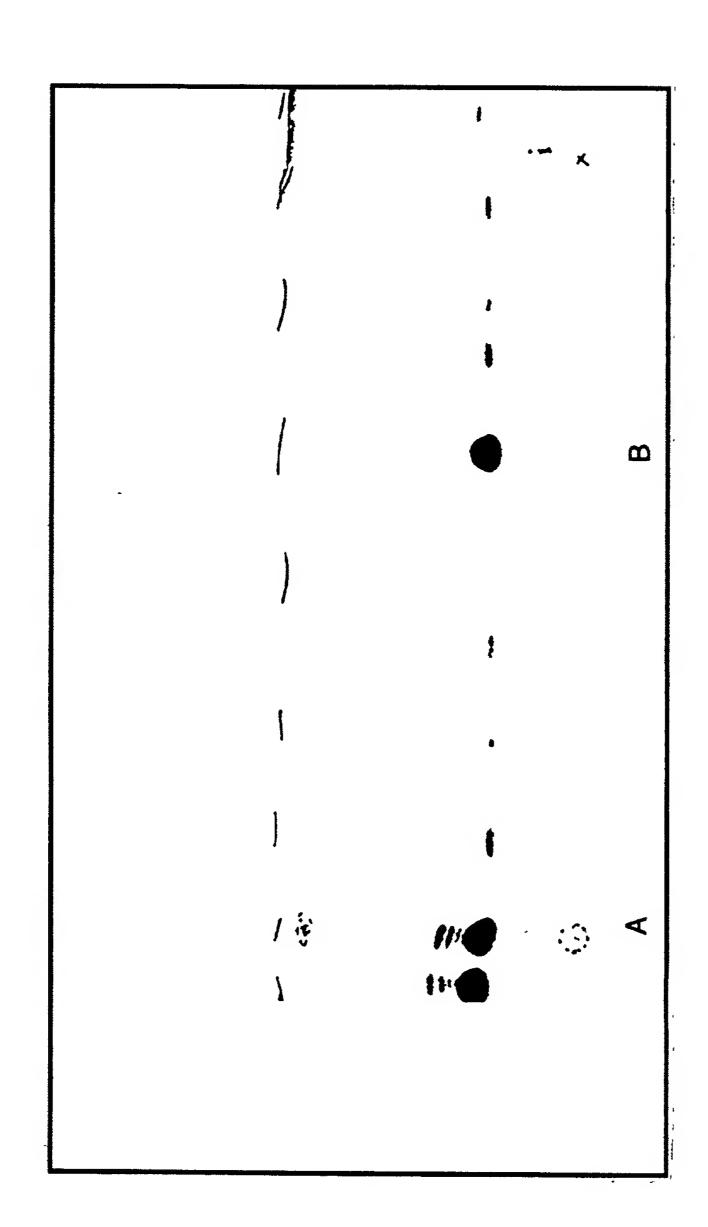
BC-Sigma

BC-Calbiochem

BC-Calbiochem

FIG. 14.

Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 15 of 35

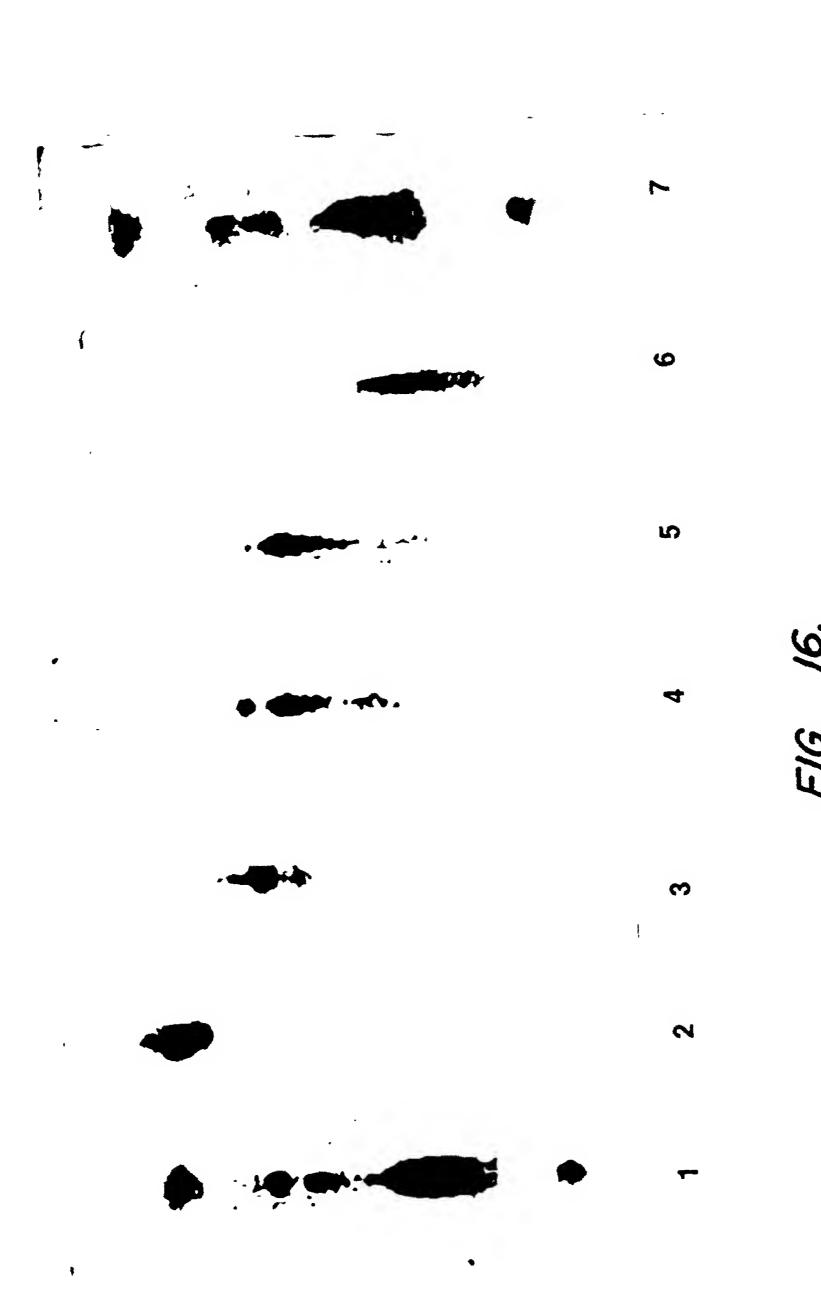


Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 16 of 35



Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 17 of 35

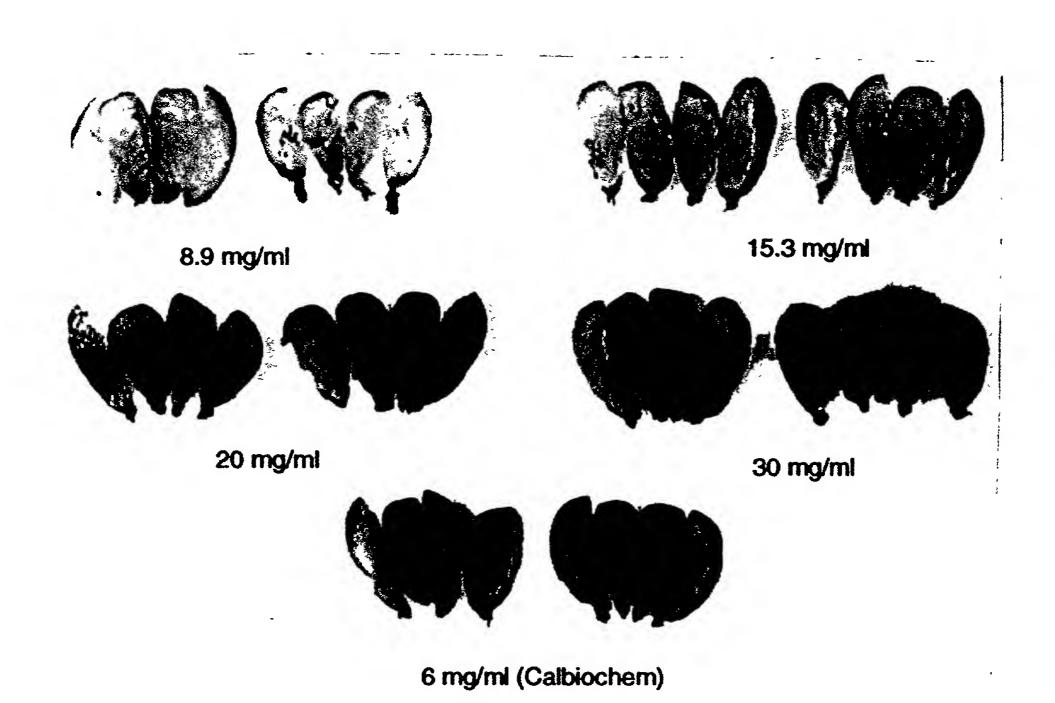


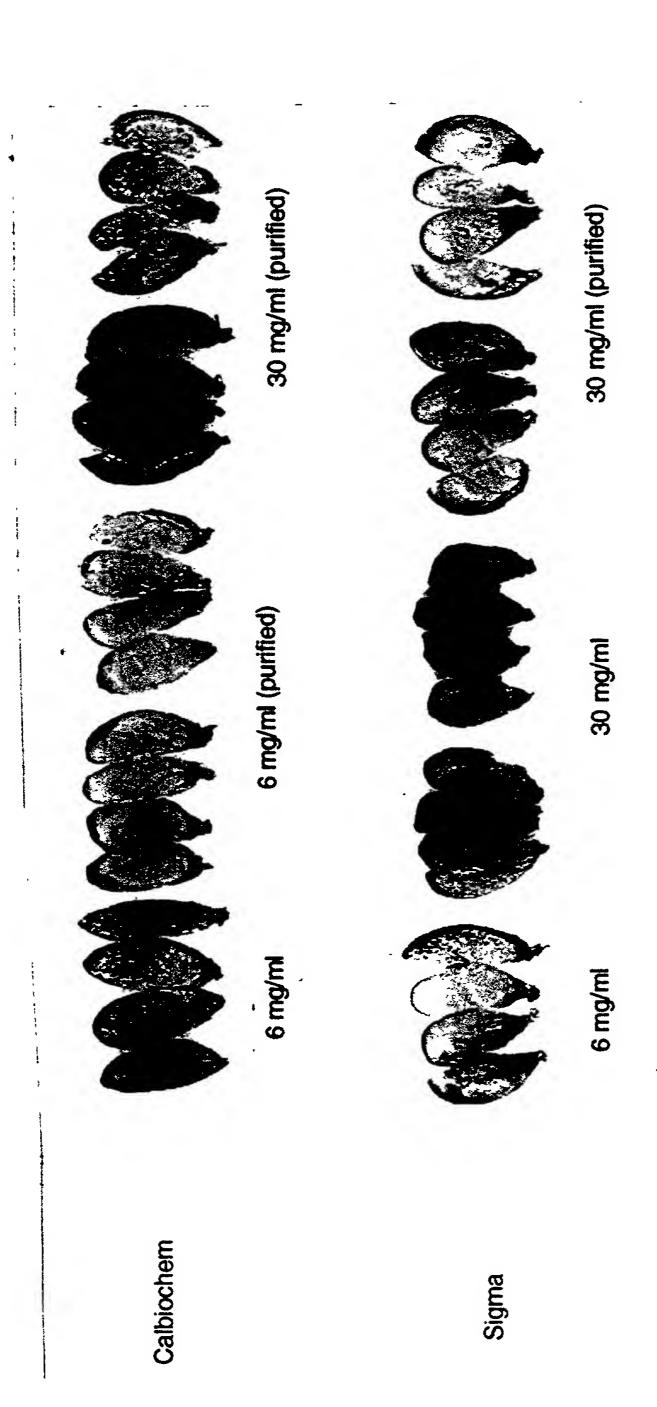
FIG. 17.

Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 18 of 35



F1G. 18

Atty. Docket No.: 016930-000816US

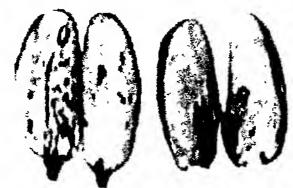
Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

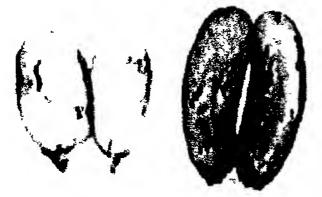
Sheet 19 of 35



6 mg/ml BC (Calbiochem)



6 mg/ml BC pure (Calbiochem)



6 mg/ml BC (Sigma)



6 mg/ml Impurity II+



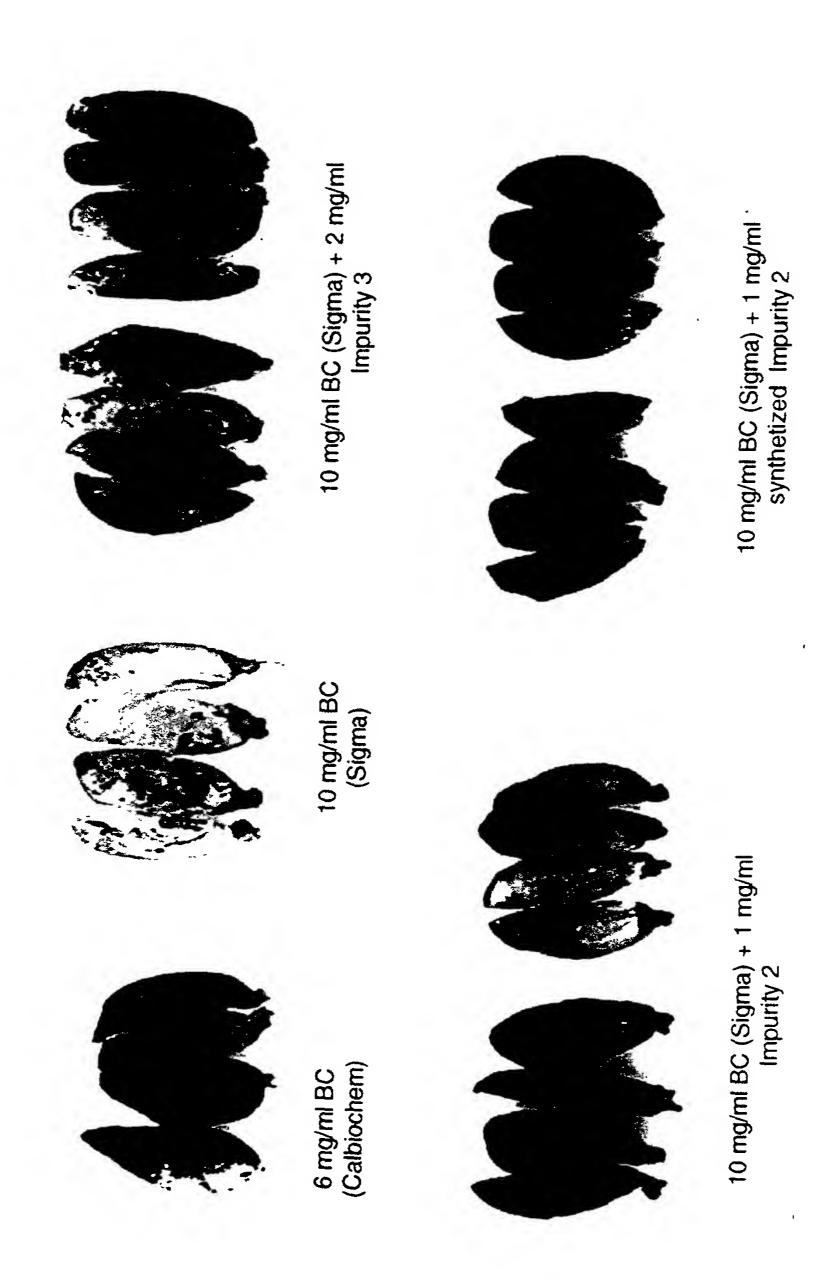
0.6 mg/ml Impurity



6 mg/ml Impurity I

FIG. 19.

Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 20 of 35



Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 21 of 35

Syn3

A-tma

A-HCl

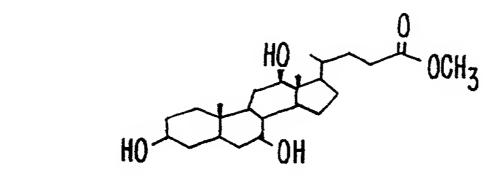
FIG. 21.

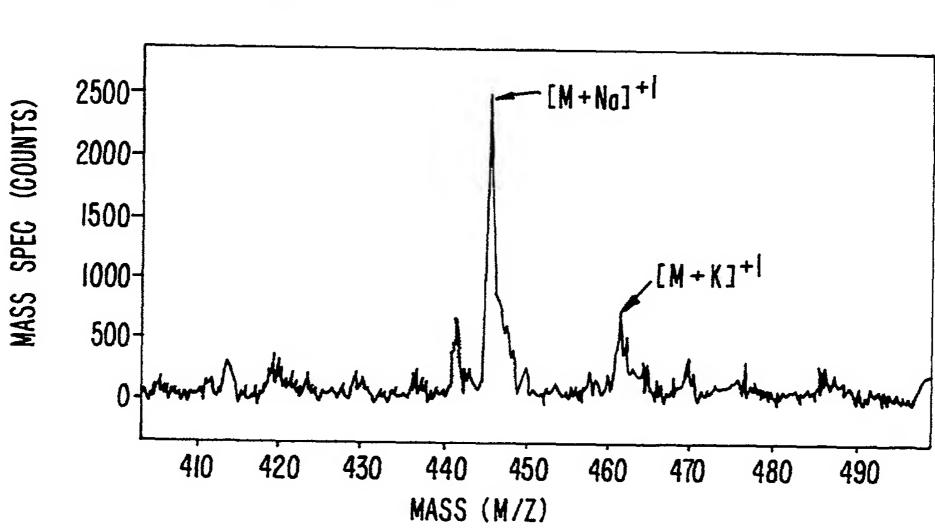
Atty. Docket No.: 016930-000816US

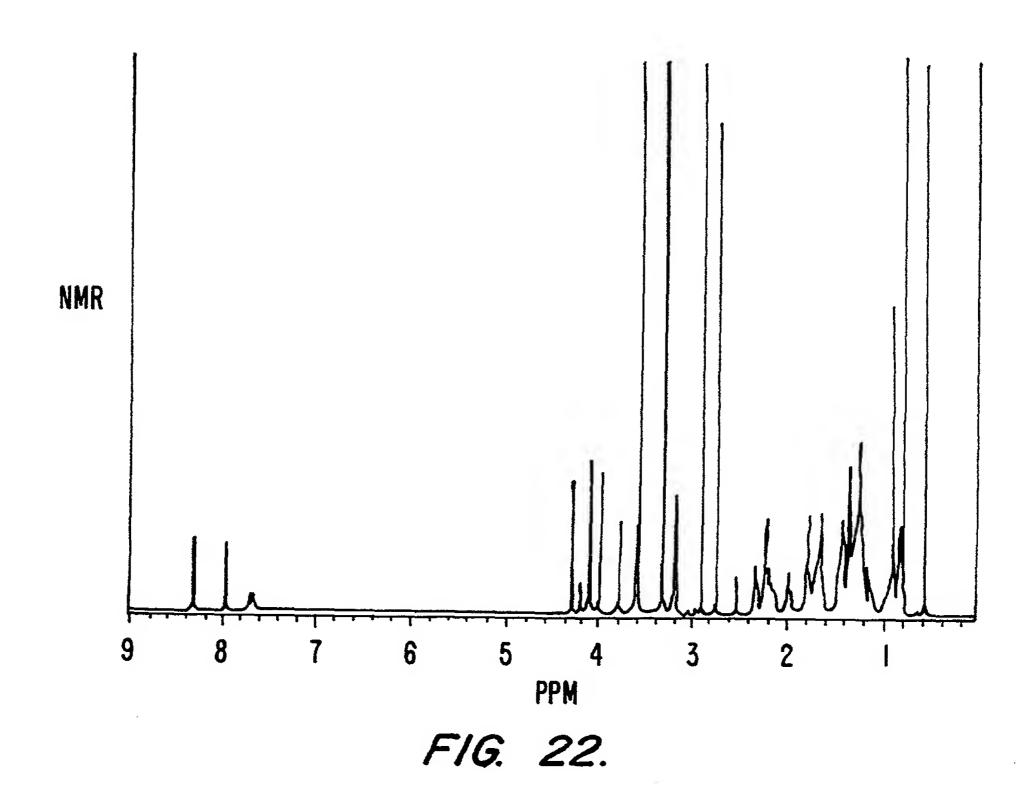
Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF

THERAPEUTIC AGENTS TO CELLS **Sheet 22 of 35**



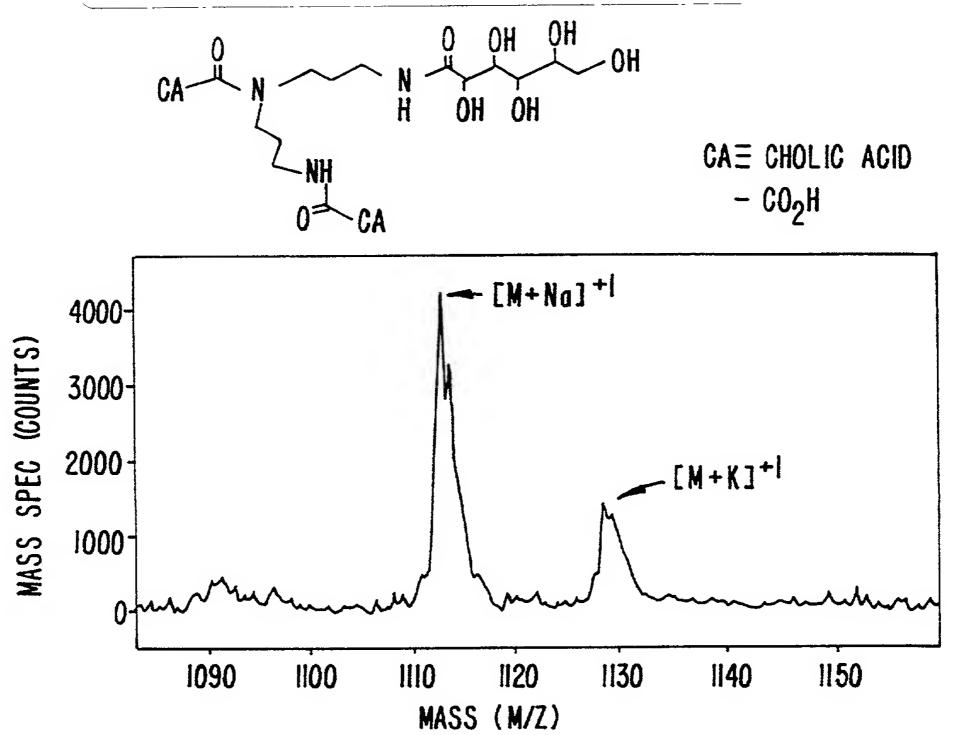




Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS **Sheet 23 of 35**



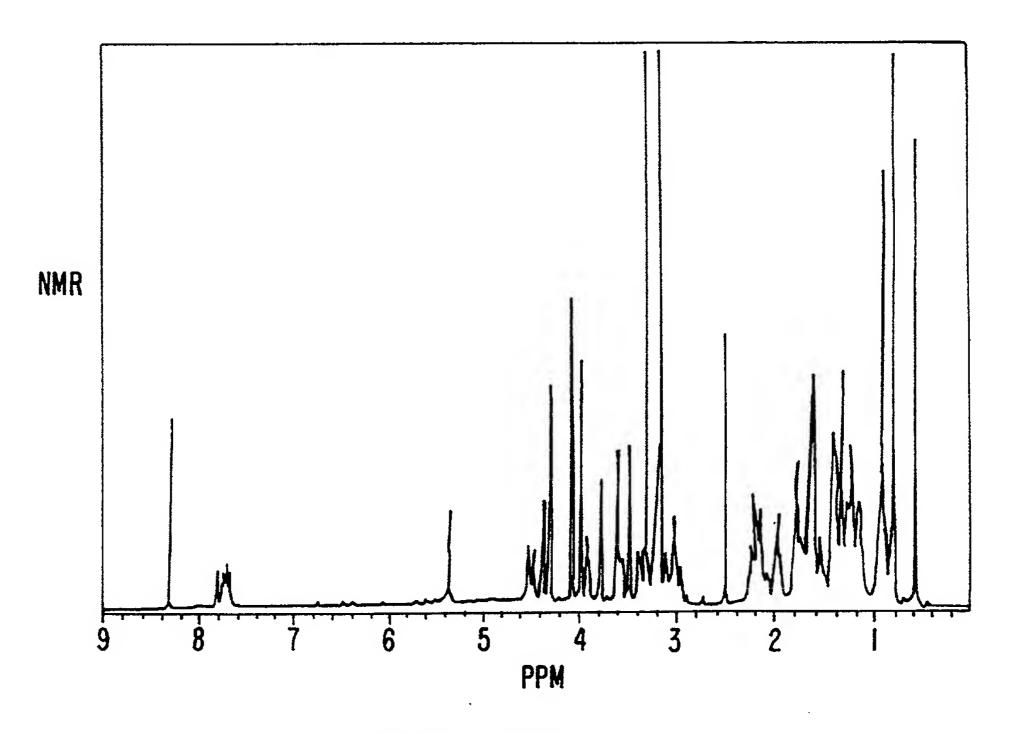


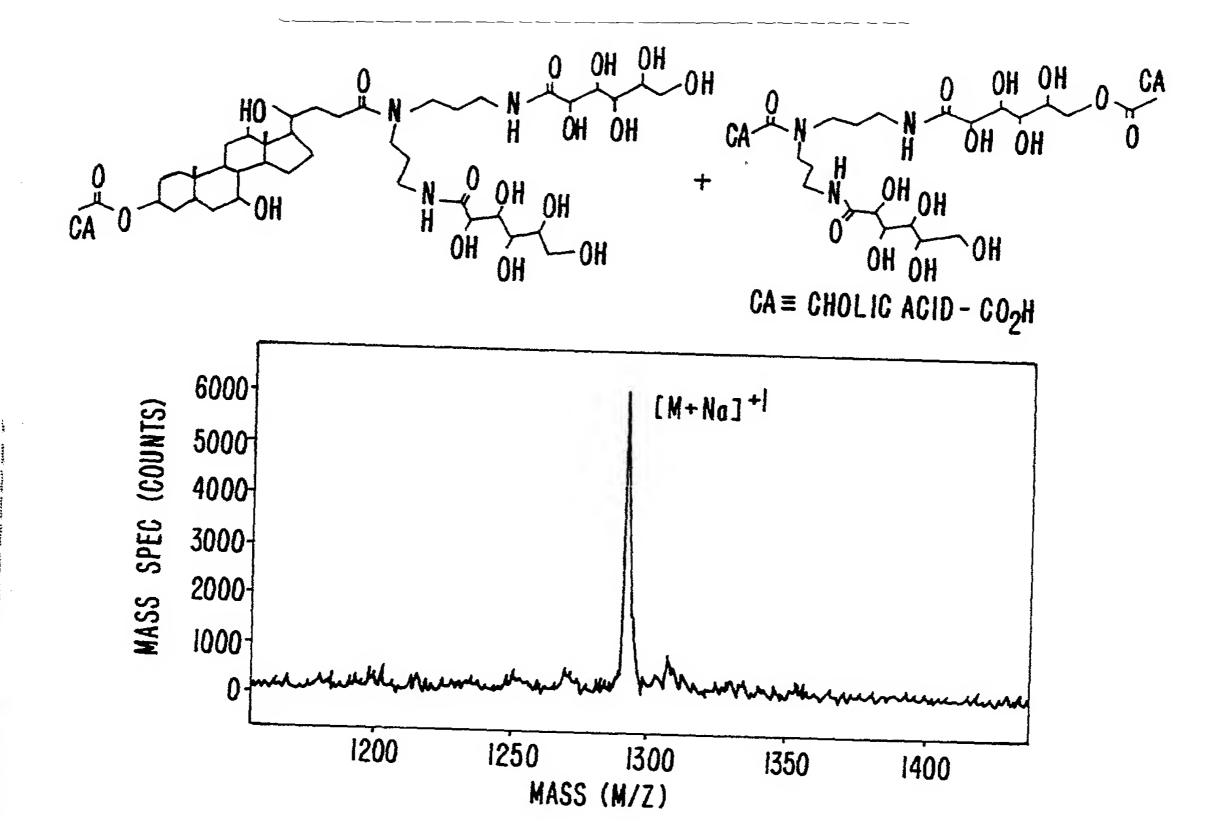
FIG. 23.

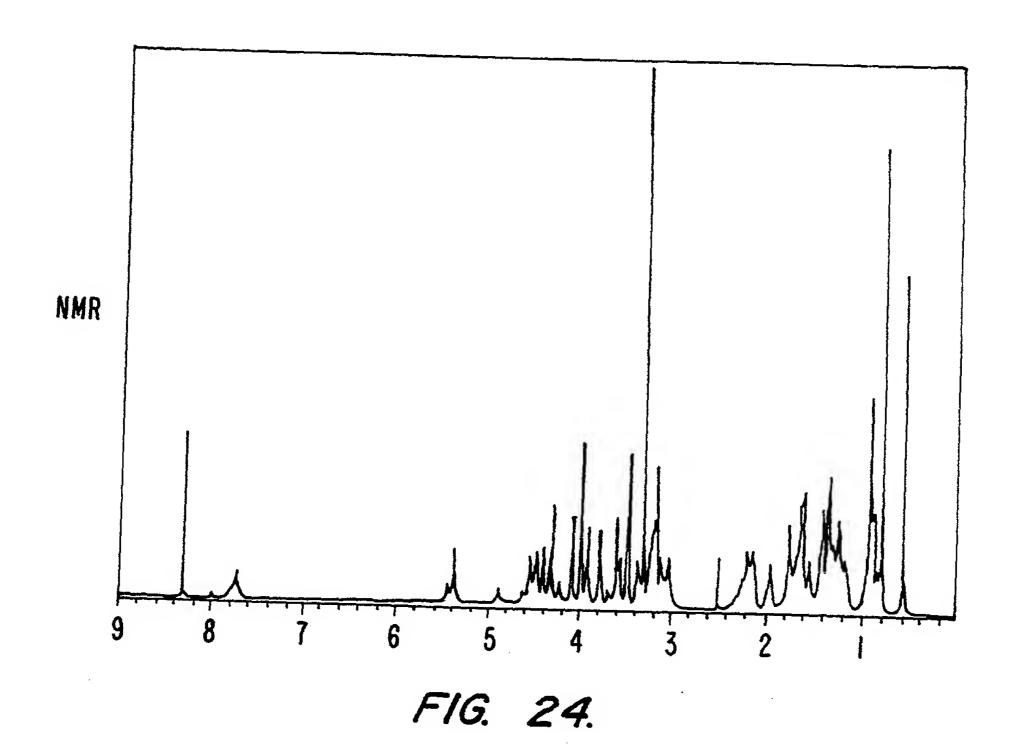
Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 24 of 35





Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 25 of 35

FIG. 25.

Impurity 2

ÓН

ÓН

Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF

THERAPEUTIC AGENTS TO CELLS

Sheet 26 of 35

FIG. 26.

Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 27 of 35

A 854 976 859 860
0.5 mg/ml I3A in 7.8 mM Big CHAP Calbiochem lot# B19546

B C C 858
977 857 978 858

Calbiochem Big CHAP Lot #B19546 Calbiochem Big CHAP Lot #679793

Figure 27

Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 28 of 35

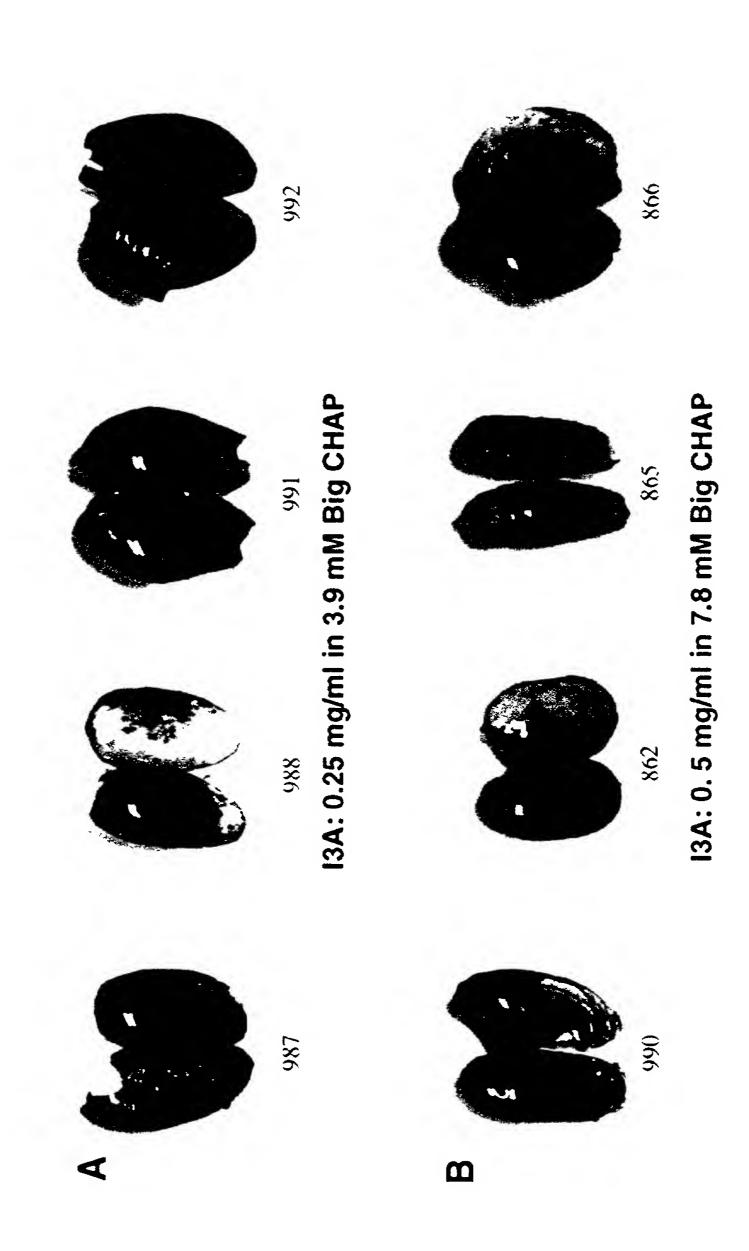


Figure 28

Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 29 of 35

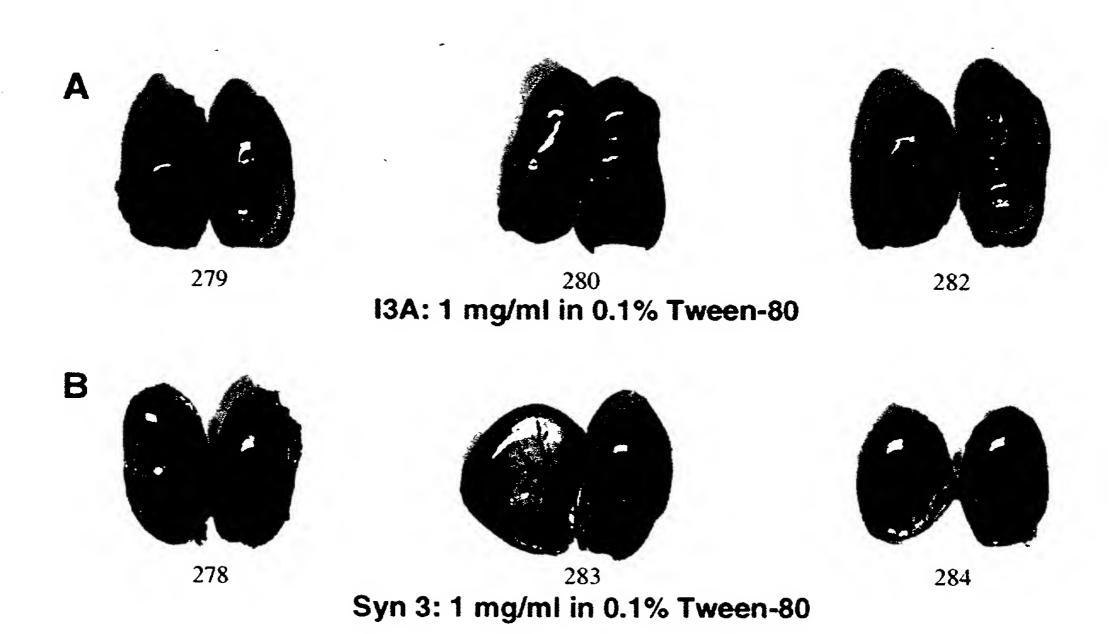


Figure 29

Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 30 of 35

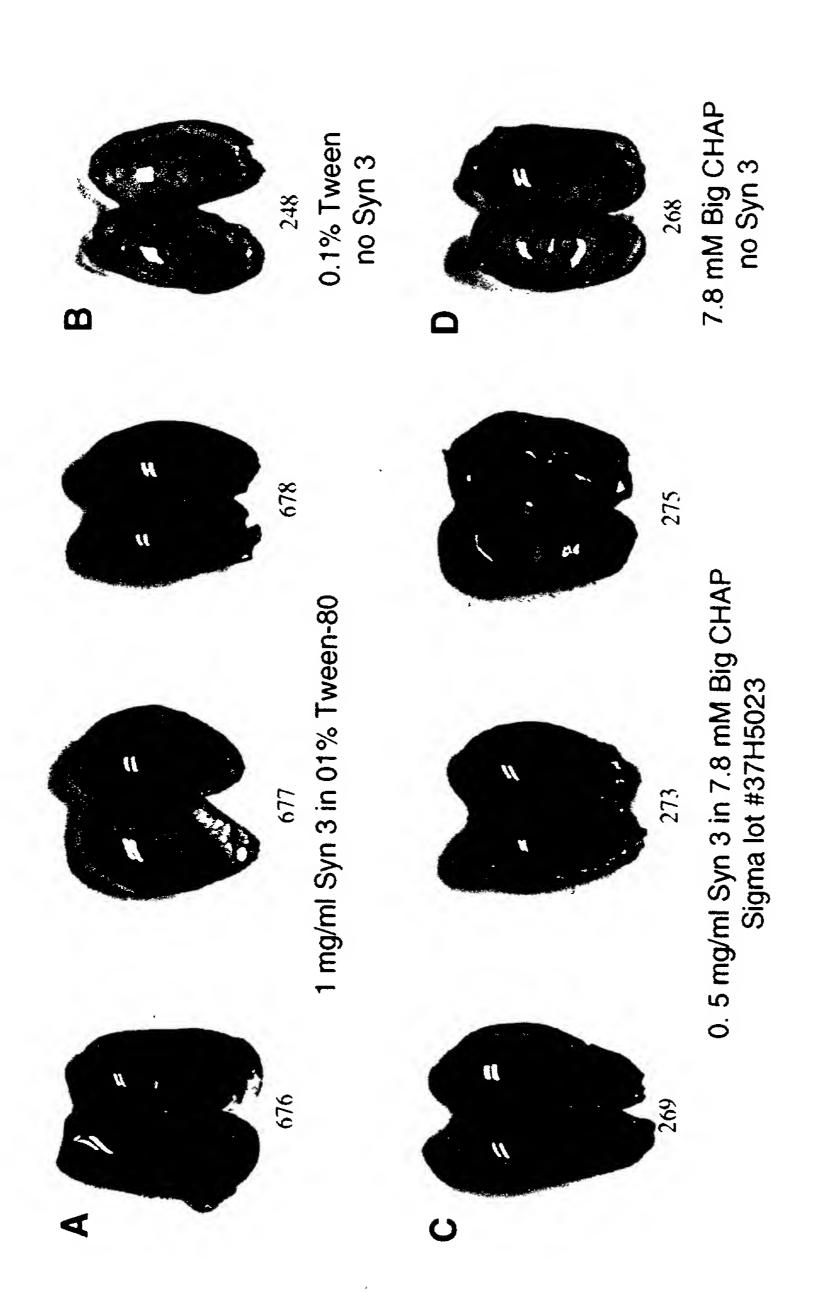
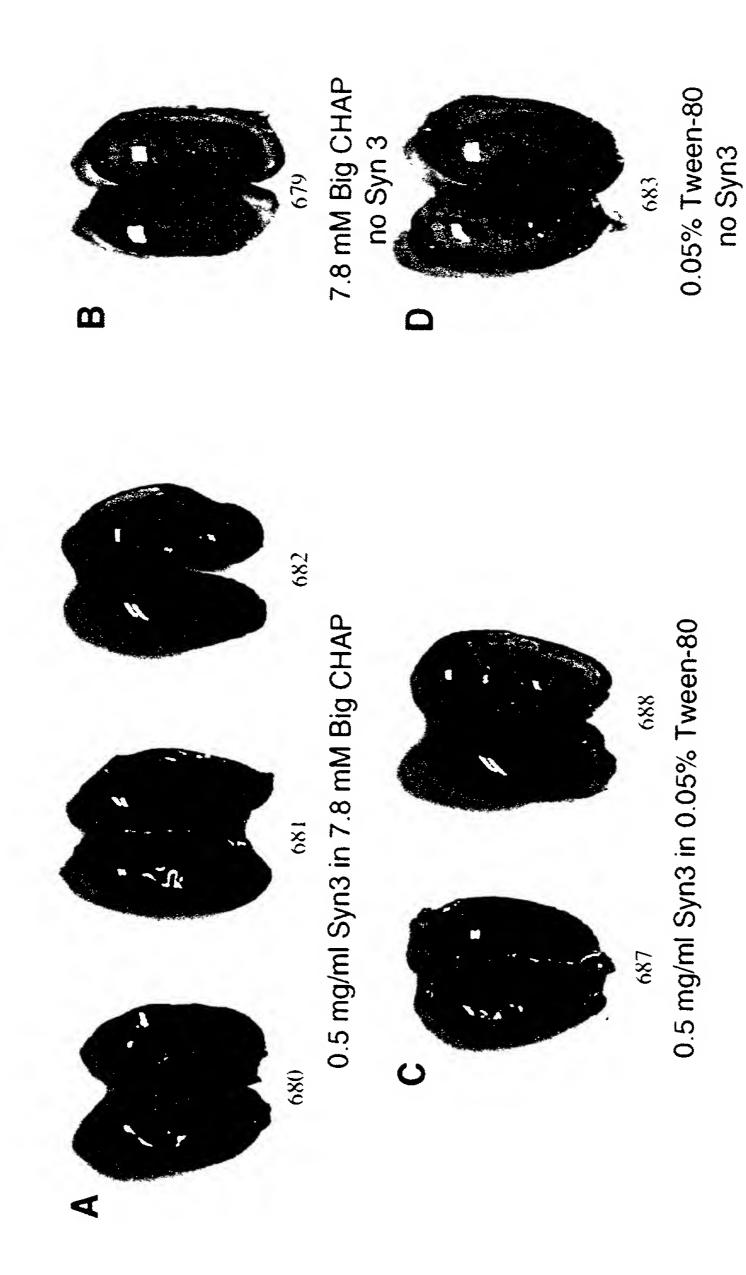


Figure 30

Atty. Docket No.: 016930-000816US Applicant: Heidrun Engler et al. Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS Sheet 31 of 35

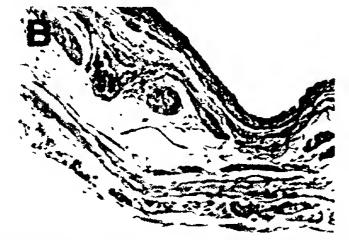


-igure 3

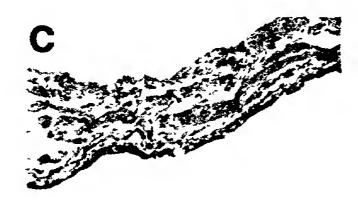
Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 32 of 35



0.5 mg/ml Syn3 / 7.8 mM Big CHAP



0.25 mg/ml Syn3 / 3.5 mM Big CHAP



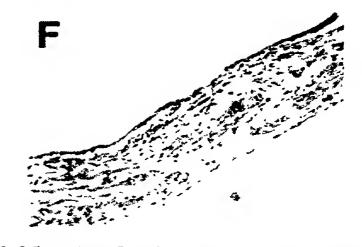
No Syn3 / 7.8 mM Big CHAP



1mg/ml Syn3 / 0.1% Tween-80



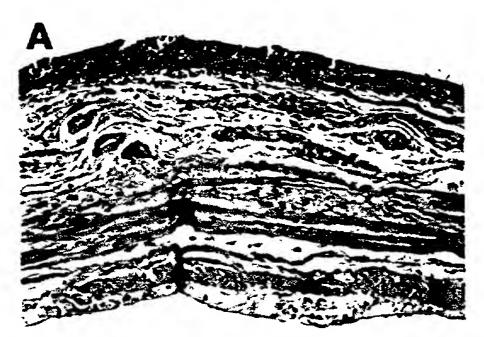
0.5mg/ml Syn3 / 0.05% Tween-80



0.25mg/ml Syn3 / 0.025% Tween-80

Figure 32

Atty. Docket No.: 016930-000816US Applicant: Heidrun Engler et al. Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS Sheet 33 of 35



Virus / Syn3 / 0.1% Tween-80



Virus / No Syn3 / 0.1% Tween-80



No Virus / Syn3 / 0.1% Tween-80



No virus / No Syn3 / 0.1% Tween-80

Figure 33

Atty. Docket No.: 016930-000816US

Applicant: Heidrun Engler et al.

Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS

Sheet 34 of 35

 $\begin{array}{c|c} \textbf{Reaction 1} & MeOH \\ reflux & from lactobionic acid / MeOH / DCC) \end{array}$

$$NH_2$$
 NH_2
 NH_2

Reaction 3 DMF 24 h

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\$$

FIG. 34.

Atty. Docket No.: 016930-000816US
Applicant: Heidrun Engler et al.
Title: COMPOSITIONS AND METHODS FOR ENHANCING DELIVERY OF THERAPEUTIC AGENTS TO CELLS
Sheet 35 of 35

FIG. 35.